

Postpartum Maternal and Neonatal Hospitalizations Among Women with HIV: A Population-Based Study

Erin M. Macdonald,¹ Ryan Ng,¹ Mark H. Yudin,²⁻⁴ Ahmed M. Bayoumi,^{1-3,5,6} Mona Loutfy,^{1,5-7}
Janet Raboud,^{1,8,9} Khatundi-Irene Masinde,⁷ Wangari E. Tharao,¹⁰ Jason Brophy,¹¹
Richard H. Glazier,^{1-3,5,9,12} and Tony Antoniou^{1,2,12}

Abstract

Postpartum maternal and neonatal readmissions in the period shortly following birth are indicators of serious morbidity. We compared the risk of postpartum maternal and neonatal hospitalizations in women living with and without HIV in Ontario, Canada. We conducted a population-based study of pregnancies in Ontario between April 1, 2002 and March 31, 2011 using Ontario's administrative health care databases. Generalized estimating equations were used to derive adjusted odds ratios (aORs) and 95% confidence intervals (CI) for the association of HIV infection with postpartum maternal hospitalizations within 30 days of hospital discharge and neonatal hospitalizations within 30 and 60 days of hospital discharge. Between 2002/2003 and 2010/2011, 1,133,505 pregnancies were available for analysis, of which 634 (0.06%) were to women living with HIV. The proportion of postpartum maternal hospitalizations (2.8% versus 1.1%; odds ratio 2.53; 95% CI 1.57 to 4.07) was higher among women with HIV. The multivariable adjusted odds ratio was 1.54 (95% CI 0.93 to 2.55). The proportions of neonates hospitalized within 30 (2.6% versus 3.7%; aOR 0.68, 95% CI 0.42 to 1.10) and 60 days (4.9% versus 4.9%; aOR 0.86, 95% CI 0.60 to 1.24) of discharge were similar among infants born to women with and without HIV. Women living with HIV are at a higher risk of postpartum maternal hospitalizations than women not living with HIV. The effect of HIV infection was attenuated by multivariable adjustment, suggesting that sociodemographic or health care factors are responsible for much of the difference in outcomes.

Introduction

POSTPARTUM MATERNAL AND NEONATAL readmissions are costly and important indicators of maternal and infant morbidity.¹⁻⁴ Existing research indicates that close to 4% of all infants are readmitted to hospital within 6 weeks of hospital discharge, while the risk of maternal readmission ranges

from 0.98% to 2.16%.^{3,5-8} Factors associated with a heightened risk of neonatal readmission include preterm and small for gestational age births, low socioeconomic status, rural residence, and young maternal age.⁵ These findings are concerning in the context of HIV infection because women with HIV are more likely to live in low income neighborhoods and their children are at higher risk of adverse neonatal

¹Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada.

²Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario, Canada.

³Centre for Research on Inner City Health, St. Michael's Hospital, Toronto, Ontario, Canada.

⁴Department of Obstetrics and Gynecology, St. Michael's Hospital and University of Toronto, Toronto, Ontario, Canada.

⁵Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada.

⁶Department of Medicine, University of Toronto, Toronto, Ontario, Canada.

⁷Women's College Research Institute, Women's College Hospital, Toronto, Ontario, Canada.

⁸Toronto General Research Institute, University Health Network, Toronto, Ontario, Canada.

⁹Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada.

¹⁰Women's Health in Women's Hands Community Health Centre, Toronto, Ontario, Canada.

¹¹Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, Ontario, Canada.

¹²Department of Family and Community Medicine, St. Michael's Hospital and University of Toronto, Toronto, Ontario, Canada.

outcomes than HIV-negative women.⁹ Similarly, the prevalence of risk factors for maternal rehospitalization, such as multiple gestation, cesarean delivery, and postoperative complications, is higher among women living with HIV relative to HIV-negative women.^{9–13}

Despite the increased prevalence of risk factors for maternal and neonatal readmissions, no studies have examined the risk and causes of rehospitalization among women with HIV and their infants in the period immediately following discharge. Such data are important for ascertaining for which women postpartum surveillance is required and whether interventions targeting potentially preventable causes of readmission are required. Accordingly, we compared the risk of maternal and neonatal hospitalizations in the first 1 to 2 months following discharge among women living with and without HIV infection in Ontario.

Materials and Methods

Setting

We conducted a population-based study of pregnancies to women living with and without HIV in Ontario between April 1, 2002 and March 31, 2011. Ontario has a universal single-payer, government administered health care system. This project was approved by the Research Ethics Board of Sunnybrook Health Sciences Centre, Toronto, Ontario.

Data sources

We used Ontario's administrative health databases, which were held securely in linkable files without any direct personal identifiers, and analyzed at the Institute for Clinical Evaluative Sciences (ICES). We identified all live births to all Ontario women between the ages of 18 and 49 years using the MOMBABY database, which deterministically links the Canadian Institute for Health Information Discharge Abstract Database inpatient admission records of all mothers and their newborn infants. Within this cohort, we identified women living with HIV using the Ontario HIV Database, an administrative data registry of Ontario residents with diagnosed HIV infection that was generated using a validated case-finding algorithm.¹⁴ The definition of three physician claims with an International Classification of Diseases, Ninth Revision code for HIV infection (042, 043, 044) within a 3-year period has a sensitivity and specificity of 96.2% [95% confidence intervals (CI) 95.2% to 97.9%] and 99.6% (95% CI 99.1% to 99.8%), respectively, for identifying persons living with HIV.

We obtained hospitalization data from the Canadian Institute for Health Information Discharge Abstract Database, which contains detailed clinical information regarding all hospital admissions in Ontario. We used the Ontario Health Insurance Plan database to identify claims for physician services such as prenatal care, and used validated disease registries to define the presence of diabetes and hypertension.^{15,16} We obtained basic demographic data from the Registered Persons Database, a registry of all Ontario residents eligible for health insurance. We adjusted for differences in comorbidity by calculating the number of John Hopkins Aggregated Diagnosis Groups (ADG) for each woman, using the John Hopkins Adjusted Clinical Group system.¹⁷ Ecologic measures of neighborhood instability and deprivation, two dimensions of the Ontario Marginalization Index, were derived using the 2006 Canadian

Census.¹⁸ We determined the adequacy of prenatal care using the Revised-Graduated Prenatal Care Utilization Index (R-GINDEX).¹⁹ The R-GINDEX is a summary measure of prenatal care, and is calculated on the basis of the number of visits for prenatal care and the trimester care began, taking gestational age into account. Finally, we ascertained immigration status and world region of origin using the Citizenship and Immigration Canada Database. These databases were linked in a coded fashion using encrypted health card numbers, and are routinely used for population-based research examining maternal and neonatal outcomes.

Outcomes

The primary outcomes were postpartum maternal and neonatal hospitalizations. We defined postpartum maternal hospitalizations as women who were discharged alive and subsequently readmitted to hospital at least once within 30 days of discharge. Similarly, we defined neonatal rehospitalizations as infants discharged alive who were subsequently readmitted to hospital at least once within 30 days of discharge; in sensitivity analyses, we also analyzed readmissions within 60 days. Transfers between hospitals were not considered readmissions.

Statistical analysis

We compared baseline characteristics of mothers living with and without HIV using one-way analysis of variance for continuous variables, Cochran–Armitage tests for ordinal variables, and chi-square tests for categorical variables. We used generalized estimating equations with a logit link function and an exchangeable correlation structure to derive adjusted odds ratios (aORs) and 95% confidence intervals (CI) for the association of HIV infection with postpartum maternal and neonatal hospitalizations. To assess the contribution of demographic and clinical risk factors for rehospitalization, we adjusted for these factors in a hierarchical stepwise manner. Specifically, we adjusted first for maternal age and comorbidity (model 1), next added socioeconomic status (model 2), followed by immigration status (model 3), and finally adding adequacy of prenatal care, mode of delivery, multiple births, and induction of labor (model 4). This selection was guided by our a priori conceptualization of the relative importance of these risk factors and their likelihood of being correlated. We also adjusted for infant birth weight and preterm birth as continuous and categorical variables, respectively, in all neonatal hospitalization models. All analyses were conducted using SAS version 9.3 (SAS institute, Cary, NC).

Results

We identified 1,133,505 pregnancies during the 10-year study period, of which 634 (0.06%) were among women living with HIV. Relative to women not living with HIV, women living with HIV were more likely to undergo caesarean section (38.5% versus 27.8%; $p < 0.001$), deliver preterm (15.8% versus 7.2%; $p < 0.001$), and live in the most deprived neighborhoods (Table 1). With few exceptions, no differences were observed between women with and without HIV with respect to complications related to labor and delivery, although the median length of admission was about a day longer for both women with HIV and their infants (Table 1).

TABLE 1. BASELINE CHARACTERISTICS

<i>Characteristic</i>	<i>HIV pregnancy n = 634</i>	<i>Non-HIV pregnancy n = 1,132,871</i>	<i>p-value</i>
Mean (SD) age at delivery (years)	30.8 (5.2)	30.1 (5.2)	0.002
18 to 34 years	458 (74.5)	881,796 (79.2)	0.002
35 to 49 years	157 (25.5)	231,463 (20.8)	
Neighborhood income quintile			
1 (lowest)	304 (47.9)	248,914 (22.0)	< 0.001
2	142 (22.4)	225,367 (19.9)	
3	66 (10.4)	230,425 (20.3)	
4	73 (11.5)	234,477 (20.7)	
5	45 (7.1)	189,324 (16.7)	
Missing	≤ 5	4,364 (0.4)	
Time since immigration			
0 to 4 years	158 (24.9)	140,121 (12.4)	< 0.001
5 to 9 years	57 (9.0)	75,641 (6.7)	
10 or more years	90 (14.2)	76,500 (6.8)	
Long-term residents	329 (51.9)	840,609 (74.2)	
Region of birth			
Africa or Caribbean	254 (40.1)	39,226 (3.5)	< 0.001
Canada	329 (51.9)	840,609 (74.2)	
Other Regions	51 (8.0)	253,036 (22.3)	
Median (IQR) maternal LOS (days)	3.0 (2.0 to 4.0)	2.0 (1.0 to 3.0)	< 0.001
Median (IQR) infant LOS (days)	3.0 (2.0 to 4.0)	2.0 (1.0 to 3.0)	< 0.001
Diabetes	12 (1.9)	20,211 (1.8)	0.836
Gestational diabetes	37 (5.8)	57,007 (5.0)	0.355
Hypertension	23 (3.6)	29,789 (2.6)	0.116
Pregnancy-induced hypertension	22 (3.5)	50,192 (4.4)	0.240
Multiple gestation	19 (3.0)	19,849 (1.8)	0.017
Preterm birth	100 (15.8)	81,047 (7.2)	< 0.001
Median (IQR) gestational weeks at delivery	38 (37–40)	39 (38–40)	< 0.001
Cesarean section	244 (38.5)	314,723 (27.8)	< 0.001
Induced labor	114 (18.0)	238,452 (21.0)	0.058
Median (IQR) prior parities	0 (0–1)	0 (0–1)	0.084
Median (IQR) aggregated Diagnosis groups	6 (5–9)	4 (3–6)	< 0.001
Revised graduated prenatal care Utilization index category			
Adequate	175 (27.6)	428,867 (37.9)	0.001
Inadequate	101 (15.9)	156,982 (13.9)	
Intensive	54 (8.5)	61,597 (5.4)	
Intermediate	304 (47.9)	484,055 (42.7)	
Missing	0 (0.0)	1,370 (0.1)	
Material deprivation quintile			
1 (least deprived)	68 (10.7)	296,868 (26.2)	< 0.001
2	72 (11.4)	233,052 (20.6)	
3	98 (15.5)	213,667 (18.9)	
4	117 (18.5)	190,959 (16.9)	
5	261 (41.2)	183,836 (16.2)	
Missing	18 (2.8)	14,489 (1.3)	
Residential instability quintile			
1 (least instability)	77 (12.1)	303,577 (26.8)	< 0.001
2	72 (11.4)	228,844 (20.2)	
3	69 (10.9)	168,458 (14.9)	
4	145 (22.9)	214,871 (19.0)	
5	253 (39.9)	202,632 (17.9)	
Missing	18 (2.8)	14,489 (1.3)	
Complications of labor and delivery			
Premature rupture of membranes	57 (8.7)	110,296 (9.6)	0.47
Obstructed labor: malposition	16 (2.5)	44,755 (3.9)	0.06
Obstructed labor: other	20 (3.1)	46,702 (4.1)	0.20
Umbilical cord complications	59 (9.0)	144,945 (12.6)	0.007
Perineal laceration during delivery ^a	186 (47.7)	467,744 (57.2)	< 0.001
Maternal placental syndromes	37 (5.8)	63,440 (5.6)	0.78
Fetal acid/base imbalance	111 (17.0)	217,147 (18.8)	0.24
Postpartum hemorrhage	29 (4.4)	42,524 (3.7)	0.31

^aDenominator is vaginal deliveries only.

HIV, human immunodeficiency virus; SD, standard deviation; IQR, interquartile range; LOS, length of stay.

TABLE 2. ASSOCIATION BETWEEN HIV AND POSTPARTUM AND POSTNATAL HOSPITALIZATIONS

Outcome	Postpartum maternal hospitalization	30-day neonatal hospitalization	60-day neonatal hospitalization
Model 1 ^a	1.92 (1.18 to 3.13)	0.64 (0.40 to 1.03)	0.85 (0.59 to 1.23)
Model 2 ^b	1.83 (1.13 to 2.98)	0.63 (0.39 to 1.02)	0.84 (0.58 to 1.21)
Model 3 ^c	1.67 (1.03 to 2.71)	0.70 (0.44 to 1.13)	0.91 (0.63 to 1.31)
Model 4 ^d	1.54 (0.93 to 2.55)	0.68 (0.42 to 1.10)	0.86 (0.60 to 1.24)

^aIncludes age and comorbidity (aggregated diagnosis groups).

^bIncludes model 1 plus socioeconomic status (material deprivation and residential instability).

^cIncludes model 2 plus immigration status.

^dIncludes model 3 plus adequacy of prenatal care, length of hospital stay, mode of delivery, multiple births, induction of labor, preterm birth (infant models only), and infant birth weight (infant models only).

The proportion of women who were hospitalized postpartum (2.8% versus 1.1%; odds ratio 2.53; 95% CI 1.57 to 4.07) was higher among women living with HIV relative to women without HIV. Overall, 44% of readmissions among women with HIV were related to infection of an obstetrical surgical wound or puerperal sepsis, compared to 10.7% of readmissions among women without HIV. Following adjustment for age and comorbidity, the risk of readmission within 30 days of discharge for women with HIV was attenuated (aOR 1.92; 95% CI 1.18 to 3.13); this risk was further attenuated following adjustment for socio-demographic and health care variables (Table 2). In the fully adjusted model, the risk was no longer statistically significant (aOR 1.54; 95% CI 0.93 to 2.55). Caesarean delivery was associated with postpartum maternal readmission (aOR 1.84; 95% CI 1.77 to 1.91). In a subgroup analysis, the risk of readmission was higher among women with HIV undergoing cesarean delivery (aOR 2.64; 95% CI 0.97 to 7.18) compared to HIV-negative women delivering by caesarean section (aOR 1.84; 95% CI 1.77 to 1.91).

The risk of neonatal hospitalizations among infants born to women with and without HIV was similar at both 30 days (2.6% versus 3.7%; aOR 0.68, 95% CI 0.42 to 1.10) and 60 days (4.9% versus 4.9%; aOR 0.86, 95% CI 0.60 to 1.24) following discharge (Table 2). Multivariable adjustment had little effect on the estimate of the adjusted odds ratio. Overall, 20 of the 42 (47.6%) hospitalizations occurring within 60 days of discharge among infants born to women with HIV were attributable to infections, including pneumonia, sepsis, and urinary tract infections.

Discussion

We found that women with HIV were at higher risk of being readmitted within 30 days of discharge following childbirth relative to HIV-negative women. This risk was attenuated following multivariable adjustment, particularly when differences in health care characteristics such as caesarean delivery were considered. In contrast, we found no difference in the risk of infant postnatal hospitalizations within 30 and 60 days of discharge. Infection was the most common cause of readmission among women with HIV and their infants in the immediate postpartum period. Our study provides the first estimate of the risk of postpartum maternal and neonatal readmissions in women living with HIV.

We speculate that the increased proportion of maternal readmissions among women with HIV reflects the greater frequency of caesarean deliveries among these women. This reasoning is supported by earlier research documenting an

80% increase in postpartum maternal rehospitalization risk among women with cesarean delivery³ and our finding that a large proportion of readmissions among women with HIV was attributable to obstetrical surgical wound infections. In addition, a meta-analysis of 10 studies found a 75% increased risk of wound infection among women with HIV undergoing a cesarean delivery relative to HIV-negative women.²⁰ Immunologic status at the time of cesarean delivery has been associated with subsequent complications in several, but not all studies.^{10,21–25} In light of these data, our findings suggest that preemptive measures may be required to reduce the burden of cesarean-related morbidity among women with HIV. Because vaginal delivery is an option for women with HIV with viral loads of 1,000 copies/ml or less,²⁶ optimizing the antiretroviral management of pregnant women with HIV could decrease the need for cesarean deliveries and prevent morbidity related to this mode of delivery. For women requiring cesarean delivery, appropriate measures, such as antibiotic prophylaxis, limiting the number of vaginal examinations during labor, and postdischarge wound care in the community, may mitigate the risk of wound complications.³

The findings of this study are strengthened by the population-based nature of the data, thereby allowing us to include all women who delivered a baby in an Ontario hospital over the 9-year study period. In addition, unlike previous studies, we were able to derive risk estimates that were adjusted for demographic and clinical characteristics that could influence the risk of postpartum readmission. However, some limitations of our study merit emphasis. As with all observational studies, it is possible that our findings partially reflect unmeasured confounders (e.g., breastfeeding rates, body mass index) or intergroup differences in the baseline risk of postpartum hospitalizations. In addition, unmeasured variables such as extent of immunosuppression and access to and adherence to antiretroviral therapy could account for within-group differences in the risk of infection among women with HIV.

We could not ascertain births that occurred outside the hospital or among women without provincial health insurance, which account for approximately 1.1% of all births in Ontario.²⁷ We also could not ascertain births among women who were refugee claimants or who did not have provincial health insurance. As noted above, our databases do not include clinical information or reliable estimates of antiretroviral drug use. Accordingly, we supplemented our data with information drawn from other sources. Specifically, a recent study of persons with HIV in Ontario who receive care at specialized HIV clinics in the province found that 76.5% of women who were in care between the years 2001 and 2011 received combination antiretroviral therapy, of whom 83%

had a suppressed viral load.²⁸ Furthermore, mean CD4 cell counts at entry to HIV care between 2007 and 2010 were 406 cells/mm³ among women aged 15 to 34 years and 340 cells/mm³ among women aged 35 to 44 years.²⁹ Finally, and of most relevance to the current study, we obtained supplemental data regarding antiretroviral therapy, viral load, and perinatal transmission from the Canadian Perinatal HIV Surveillance Program (extracted for 614 births to women living with HIV in Ontario for the period covered by our study), which indicates that 86.5% of women with HIV received combination antiretroviral therapy, and only 8.5% received no therapy during their pregnancy (Canadian Perinatal HIV Surveillance Program, personal communication). The proportion of women receiving antiretroviral therapy during pregnancy increased over time, from 83% in 2006 to over 90% for the period encompassing the years 2007 to 2009.²⁹ Of the women on combination antiretroviral therapy, the risk of vertical transmission was 1.1%. Viral load data were available for 91% of women during the period encompassing 2006 to 2011, of whom 82.8% attained virologic suppression below the limits of detection (50 copies/ml), with a further 10.3% being suppressed to less than 1,000 copies/ml (Canadian Perinatal HIV Surveillance Program, personal communication). Although we were not able to capture CD4⁺ count at delivery, these data indicate that most women were on antiretroviral therapy, virologically suppressed, and appropriately managed in terms of their HIV infection.

In conclusion, greater proportions of women with HIV are readmitted to hospital within 30 days of discharge following childbirth relative to HIV-negative women and infection of surgical obstetric wounds was the most common reason for these admissions. There was no significant difference in the proportion of infants born to women with and without HIV who were rehospitalized within 30 and 60 days of discharge. Further research aimed at optimizing postpartum infection control and characterizing the clinical characteristics of women with HIV readmitted to hospital will further clarify where areas for intervention exist for preventing such readmissions.

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Author Disclosure Statement

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Address correspondence to:

Tony Antoniou
410 Sherbourne Street
Toronto, Ontario M4X 1K2
Canada

E-mail: tantoniou@smh.ca